

AMENDMENTS TO THE CLAIMS

Claims 1-29 (Canceled)

30. (Currently amended) A transgenic mouse embryo whose genome comprises a homozygous disruption in the endogenous mouse ubiquitin ligase E3 gene set forth in SEQ ID NO:1, wherein ~~where the disruption is homozygous~~ the transgenic mouse embryo lacks production of functional protein encoded by the gene set forth in SEQ ID NO:1 ~~endogenous mouse delta opioid receptor~~, and exhibits increased incidence of lethality during embryonic development, relative to a wild-type mouse.
31. (Currently amended) The transgenic mouse embryo of claim 30, wherein the increased incidence of lethality occurs at approximately embryonic day 8.5.
32. (Currently amended) The transgenic mouse embryo of claim 30, wherein the increased incidence of lethality during embryonic development comprises arrested development after embryonic day 8.5.
33. (Currently amended) The transgenic mouse embryo of claim 30, wherein the transgenic mouse embryo comprises small, abnormal or reabsorbing egg cylinders.
34. (Canceled).
35. (Currently amended) The transgenic mouse embryo of claim 33, wherein the egg cylinders are reabsorbed by embryonic day 8.5.
36. (Currently amended) The transgenic mouse embryo of claim 35, wherein the abnormal egg cylinders at embryonic day 8.5 resemble egg cylinders of a normal embryo at embryonic day 7.5.
37. (Currently amended) A cell or tissue obtained from the transgenic mouse embryo of claim 30.
38. (Canceled)
39. (Currently amended) A method of producing a transgenic mouse embryo comprising a homozygous disruption in the endogenous mouse ubiquitin ligase E3 gene set forth in SEQ ID NO:1, the method comprising:
- (a) introducing a ubiquitin ligase E3 targeting construct into a mouse embryonic stem cell which targets the sequence set forth in SEQ ID NO:1;
 - (b) introducing the mouse embryonic stem cell into a blastocyst;
 - (c) implanting the blastocyst into a pseudopregnant mouse, wherein the pseudopregnant mouse gives birth to a chimeric mouse; and

(d) breeding the chimeric mouse to produce a transgenic mouse embryo comprising a homozygous disruption in the a ubiquitin ligase E3 gene;
wherein ~~where the disruption is homozygous,~~ the transgenic mouse embryo lacks production of functional mouse ubiquitin ligase E3 protein encoded by SEQ ID NO:1 and exhibits increased incidence of lethality during embryonic development, relative to a wild-type mouse.

40. (Currently amended) The transgenic mouse embryo produced by the method of claim 39.